February 4, 2020

Stephen Hahn, MD
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: FDARA Implementation Guidance for Pediatric Studies of Molecularly Targeted Oncology Drugs: Amendments to Sec. 505B of the FD&C Act Guidance for Industry

Dear Dr. Hahn:

On behalf of the thousands of children with cancer, their families and those who have yet to be diagnosed, the Children's Cancer Cause (CCC) would like to take this opportunity to comment on the proposed FDARA implementation guidance for industry on pediatric studies of molecularly targeted oncology drugs. We would also like to commend FDA for its conscientious and thoughtful response to the requirements of the Act.

The Children's Cancer Cause, established in 1999, was founded to ensure the needs and perspectives of children with cancer and survivors are integrated into federal health care, research and cancer policy. In this role, CCC has been a leading advocate for regulations that could advance pediatric oncology drug development. From the passage of the Best Pharmaceuticals for Children Act (BPCA) in 2002, the enactment of the Pediatric Research Equity Act (PREA) in 2003 and their effectiveness in FDA reauthorizations in 2007, 2012 and 2017, CCC has increasingly urged policy makers to address the inadequacies of PREA that allowed for open-ended waivers for the evaluation of new oncology agents in pediatric clinical trials in conjunction with New Drug Applications (NDA) and Biologic Licensing Applications (BLA).

Starting in 2012, CCC worked with clinical leaders, regulators and advocates to give FDA the authority to require companies to evaluate oncology agents intended for adults when new scientific findings indicate that they might have therapeutic effect in children. In addition, given that all childhood cancers are orphan diseases, we worked to remove the automatic orphan drug exclusion from PREA for cancer drugs, allowing FDA to require pediatric evaluation of cancer drugs. The passage of FDARA in 2017 represents a long-overdue shift in the rationale and requirements for pediatric clinical trials for all new cancer drug applications in

development for adults which are molecularly relevant for the disease process in childhood malignancies.

Several features of the guidance are worth noting especially as they promote efficient planning and prevention of duplication. The guidance features alternative trial designs for pediatric studies, recognizing the challenges of diminishing numbers of eligible patients due to molecular subdivisions of disease. Accordingly, the FDA is to be commended for stressing international collaboration agreements about pediatric plans with the European Medicines Agency (EMA) and regulatory agencies from other countries. Hopefully, such coordination will encourage companies to advance international alignment and prevent duplication in planning pediatric oncology trials. We are especially pleased that the European-based ACCELERATE project is cited as a trusted forum in which regulators, industry representatives, clinicians and patient advocates can collaborate to define further the parameters of molecularly driven pediatric cancer evaluations.

FDA states that it will consider pediatric waivers for agents within the class when competing studies with the same mechanisms of action have already been undertaken and there is no evidence that next in class agents would be more effective. This approach clearly will protect children from unnecessary exposure to agents for which there may already be effective therapy. It may also prevent companies from conducting pediatric trials of agents that do not propose clinical advances for children but rather fulfill a pediatric requirement for the sole purpose of seeking extended exclusivity for an adult indication.

We are also pleased to see the guidance describe a clear pathway for FDA to issue a Written Request once an Initial Pediatric Study Plan (iPSP) and Proposed Pediatric Study Request (PSP) are evaluated. We would hope that the "carrot" of a possible six months of marketing exclusivity for a new agent will work in the new regulatory context to incentivize companies to move early and efficiently to gather the evidence necessary for submitting pediatric plans.

CCC would like to urge the Agency to be strict with the timelines and deadlines for iPSP and PSPs. While we understand these timelines are required in iPSP applications, we urge FDA to strongly encourage companies to thoroughly investigate academic, NCI, NIH and other resources necessary to provide evidence for their pediatric plans in a timely manner. Similarly, if an applicant is awarded a deferral or waiver, a determination of when that designation might be revisited, or not, would require industry to be vigilant about emerging

scientific developments related to pediatric oncology and would help guide companies' planning.

In conclusion, CCC is encouraged by the thoughtful and comprehensive approach FDA has taken in the implementation of Amendments to Sec. 505B. The guidance places the goal of advancing children's access to new and potentially effective therapies first and provides industry with more certainty about regulatory expectations in this new era of molecularly based therapies.

We look forward to continuing our collaboration with FDA and other stakeholders.

Sincerely,

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